REMARKS

The title has previously been amended more accurately to reflect the nature of the invention. However, since it seems that this amendment may not have been entered, the request for amendment of the title is resubmitted herein.

Claims 3 and 10 now stand rejected over the combination of Galli *Nephrology, Dialysis Transplantation* in view of Zaloga US patent 6,060,446 and Droge et al US 5,607,974.

As noted by the Examiner, the newly-cited Galli reference makes no reference of the use of cystine or cysteine at all. Galli teaches that apoptosis that occurs in peripheral blood mononuclear leucocytes in patients on dialysis may be countered by use of vitamin E or thiol suppliers. Reference is made to incubation of leucocytes with such compounds as vitamin E and N-acetyl cysteine. That is to say an environment in which there is direct contact between the compounds being used and the cells whose apoptosis is to be reduced. There is no suggestion that anything could be administered orally The only *in vivo* testing involved use of Vitamin E-treated dialysis membranes to treat hemodialysis patients. (See page 1599 lower left hand column). Nothing in this suggests oral administration of anything. It certainly does not point to oral administration of cystein or cysteine, compounds which are not even mentioned in the article. As noted in response to previous actions, teaching of the use of N-acetyl cysteine whatever its means of administration cannot be equated with a teaching to use cysteine as required by the present claims.

Zaloga teaches that acute renal failure may be traeted by use of a composition comprising protein, amino acids and peptides. Prophylactic use is also suggested. A mixture of amino acids seems required. Cysteine is listed as one of the amino acids and is stated to have a cyto protective effect. Cystine is not mentioned. There is no suggestion of using the mixture in combination with hemodialysis.

The Dröge reference has been discussed in detail in response to previous actions. It adds nothing relevant to Galli or Zaloga. It teaches that patients having a cysteine deficiency may beneficially be treated with a cysteine source that is capable of being transported across the

cellular membrane and includes N-acetyl cysteine in the list of compounds that may act as this source. Cysteine itself is not listed. (See column 2 lines 30 - 35). The examiner comments that "Droge's teaching encompasses the administration of 'any drug' that can be transported into the cytoplasm of the cell and/or elevate plasma thiol levels to provide cysteine". However, nothing indicates that orally-administered csteine meets this requirement. Where, as in Droge, it is taught that the objective is to raise the levels of a compound in a cell and the list of compounds given as being capable of doing this excludes the compound itself, one has to believe that the exclusion was deliberate. As pointed out in some detail in response to the previous action, cysteine and N-acetyl cysteine have different pharmacological properties. The examiner cannot therefore just assume that cysteine itself would be a suitable "cysteine source for Dröge's purposes when Dröge himself does not say so. As pointed out previously, Droge is seeking to insert cysteine into liposome lumens so that it can result in an increase of the thiol level in blood plasma. Nothing in this suggests that cysteine itself should be used for this.

Putting these references together therefore, the most that can be said is that Zaloga teaches that some benefit can be achieved by a cysteine-containing mixture and this is helpful as a nutritional composition for treating acute renal failure. Galli teaches that apoptosos of mononuclear nucleocytes in hemodialysis patients may be inhibited by use of vitamin E or thiol suppliers and uses vitamin E-coated dialysis membranse for this purpose and Droge teaches treatment of cysteine defficiency in a variety of patients, inculding patiients on hemodialysis with compounds that will transport cysteine across the cell wall but conspicuously omits cysetine itself from the list of useful compounds.

Nothing here points towards the use of orally administered cysteine to treat conditions arising from dialysis. The only reference to using cysteine itself is in Zaloga and this simply suggests incuding cysteine in a complex mixture as a nutritional with no reference to hemodialysis. This combination of references does not point to using oral cysteine to treat oxidative shock arising from hemodialysis.

It is therefore submitted that the requirements of 35 USC 103 have been complied with and that this application should be allowed.

Respectfully submitted,

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